EXHIBIT C

MICHAEL KARRAM MD FACOG FPMRS
UROGYNECOLGY AND GYNECOLOGIC SURGEON
SEVEN HILLS WOMENS HEALTH CENTERS
CINCINNATI, OHIO

General TVT Report Prepared by Michael Karram MD FACOG FPMRS

Education, Training and Experience:

1973:	BS Ohio State University Columbus, Ohio
1978:	MD Cairo University Faculty of Medicine (Honors) Cairo Egypt
1979-80:	Internship Case Western Reserve Cleveland Ohio
1980-84:	Residency Good Samaritan Hospital Cincinnati, Ohio
1983:	Two week clerkship in Urogynecology with Dr. Donald Ostergard Long Beach Memorial Hospital
1984-2001:	Obstetrics and Gynecology Private Practice Cincinnati, Ohio
2001-Pres:	Gynecology Practice focusing on gynecologic surgery and Urogynecology
1986:	Board Certification, American College of Obstetrics and Gynecology
1986:	Diplomate, American Board of Obstetrics and Gynecology
2014:	Board Certification, Female Pelvic Medicine and Reproductive Surgery
1998-Pres:	Director, Urogynecology Seven Hills Women's Health Centers Cincinnati, Ohio
2013-Pres:	Director, Fellowship Minimally Invasive Gynecologic Surgery, Christ Hospital Cincinnati, Ohio
2015-Pres:	Medical Director Pelvic Floor Center Mercy West Hospital Cincinnati, Ohio
1998-2013:	Consultant, Proctor, Preceptor and Trainer for Ethicon/Gynecare
2000-Pres:	Consultant, Proctor, Preceptor and Trainer for American Medical Systems (Astora)
2013:	Presenter at AUGS meeting
2015:	Presenter at AUGS meeting

Member American Urogynecoloic Society (AUGS)
Member International Urogynecologic Association (IUGA)
Member American Association of Gynecologic Laparoscopists (AAGL)

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I am nationally and internationally known in the field of gynecologic surgery and advanced pelvic surgery. As an expert at treating both stress incontinence and pelvic organ prolapse, I have extensive experience using native tissue and augmented repairs. I have been performing TVT since 1998 and have experience with retropubic, transobtrurator, and single incision slings. I have also performed a large number of mesh augmented pelvic organ prolapse surgeries.

As a consultant for the above listed companies I participated as lead faculty at many sling courses and mesh augmented prolapse courses. These courses would include a didactic portion and a cadaver training portion. A lengthy discussion on indications, techniques, complications, management of complications and consenting patients correctly would follow each session. Upon completing these course participants were well versed in:

- Patient selection
- Correct consent process
- Understanding the IFU of the product/products
- Surgical technique
- Implant the procedure completely on the cadaver
- Understand possible complications and how to manage them
- When to refer complicated or difficult patients

Experience:

I have been performing incontinence surgery my entire career, and have employed all the surgical procedures. I have found the TVT to be the most beneficial to patients. It has excellent results, is a minimally invasive procedure, has quick patient recover, is very reproducible, and has excellent outcomes. Additionally, I have extensive experience teaching

residents and fellows on the risks and benefits of surgical treatment for stress urinary incontinence and pelvic organ prolapse, including training on the Instructions for Use (IFU).

There is no comparison to the more invasive techniques we have used prior to the TVT. Since 1998 it has been my primary surgery unless clinical situations dictate differently. I have taught this procedure to many surgeons both nationally and internationally, and have personally performed over 2000 slings. Because of all the reasons stated, I will continue to use TVT as my preferred method to surgically correct stress urinary incontinence (SUI). In summary, in my opinions discussed below, the TVT's design and material is reasonably safe for its intended use and the Instructions for Use adequately and appropriately warns physicians trained in the surgical treatment of stress urinary incontinence of the potential adverse reactions associated with the device.

The rates for my services are:

Review of records/conference (per hour)	$500.00
Deposition in town (per hour) minimum	$3,000.00
Deposition out of town (per hour) minimum	$4,000.00
Court time (per hour)	$600.00
In town minimum	$3,000.00
Out of town minimum	$4,000.00
Cancellation of deposition/court prior to 5 working days	$00.00
Cancellation within 5 working days	$2,000.00
Travel and other expenses	Billed separately

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History of Urinary Incontinence:

It is estimated that 25%-75% of women will report some form of urinary incontinence. Minassin et al. (2008) reported that 23%-38% of the female populations in the United States older than age 20 admit to symptoms of stress urinary incontinence. Approximately 16% of patients report their incontinence to be of moderate severity. It is estimated that 7% -10% perceive the SUI as severe. Analysis of Medicare data suggests that only approximately 10% of women diagnosed with SUI undergo surgical correction. Based on population growth charts, it is estimated that the number of women with urinary incontinence will increase from 18 million to 28 million women from 2010-2050.

The pathophysiology of SUI is related to the anatomic position and health of the urethra. Anatomically, the urethra has to be in the right position and well supported during times of stress or strain. If these conditions are not met, then there is excess movement of the urethra and you have a condition of hypermobility. The urethra has a blood and nerve supply that keep its' functional integrity intact. Disruption to the integrity will lead to a urethra that cannot close effectively a condition called lead pipe urethra. This is commonly labeled intrinsic sphincter deficiency (ISD).

Risk Factors for SUI:

Risk factors for SUI can therefore be those that affect one or both of the above described mechanisms. Multiple risk factors have been proposed and studied. These include age, parity, vaginal delivery, hysterectomy, pelvic and vaginal surgery, obesity/BMI, diabetes,

hormone replacement therapy, hysterectomy, physical activity, smoking, diet, other medical conditions, and family history (genetic predisposition).

Work-up of the Incontinent Patient:

The workup for an incontinent patient involves demonstration of incontinence on a cough stress test, normal post void residual, rule out urinary tract infection, a positive Q-tip test and a normal voiding pattern. The Q-tip test is performed by placing a Q-tip in the urethra at the level of the urethra-vesical junction (bladder neck). The angle of the Q-tip to the floor is then measured both at rest and as the patient coughs and strains. If the angle is between 30 and 45 degrees or greater, this indicates a hypermobile urethra. An angle that is less than 30 degrees or non- existent indicates a non-mobile urethra. This information is important when deciding what therapy is used for SUI. In cases that are more complicated, there is a question of overactive bladder associated with the SUI, or to diagnose intrinsic sphincter deficiency, the physician may elect to perform urodynamic testing.

Management of SUI:

The management of SUI has evolved dramatically, both from a patient and surgeons perspective. Historically, patients would not seek treatment because they were told ‘this is a natural part of aging, you just have to live with it’. Or, ‘there is no effective treatment and the treatments that are available are complicated, require long recovery, and always fail’. Many women suffered in silence because of these beliefs.

As women and their healthcare providers became more informed and technology progressed many patients actively pursued management of their condition. The management

was either non-surgical or surgical. Women who were not affected by their condition from a quality of life aspect usually did nothing or tried to conservatively manage their issues. This included fluid restriction, frequent bathroom visits, avoiding activities that precipitated incontinence episodes, and wearing absorbent pads. There were also incontinence pessaries and other mechanic devices that could be used as an obstructive management of incontinence.

Surgery remained the mainstay for the treatment of SUI; however it has significantly evolved over the years due to innovation and better understanding of the disorder. . It is well known by all pelvic floor surgeons that any surgery for stress urinary incontinence or pelvic organ prolapse, with or without the use of mesh, can potentially cause complications that can be temporary or permanent, including but not limited to: pelvic pain, dyspareunia (pain with sexual intercourse), scarring, vaginal narrowing, leg/groin pain, urinary retention and other voiding problems. Historically, there have been many surgeries that have been used to treat SUI, culminating in the mid-urethral sling used today. Most experts in the field of female pelvic medicine and reconstructive surgery agree that the mid-urethral sling is the standard of care for the treatment of SUI. Support is based on an abundance of scientific data. The American Urogynecologic Society (AUGS) performed a worldwide survey of its members asking 'what is your procedure of choice for surgical management of SUI'. The overwhelming majority answered a mid-urethral synthetic sling.

Surgical procedures for SUI:

Anterior repair/cystocele repair: For many years this was the procedure used to treat SUI. It was designed to repair an anterior vaginal wall defect that allowed the bladder to

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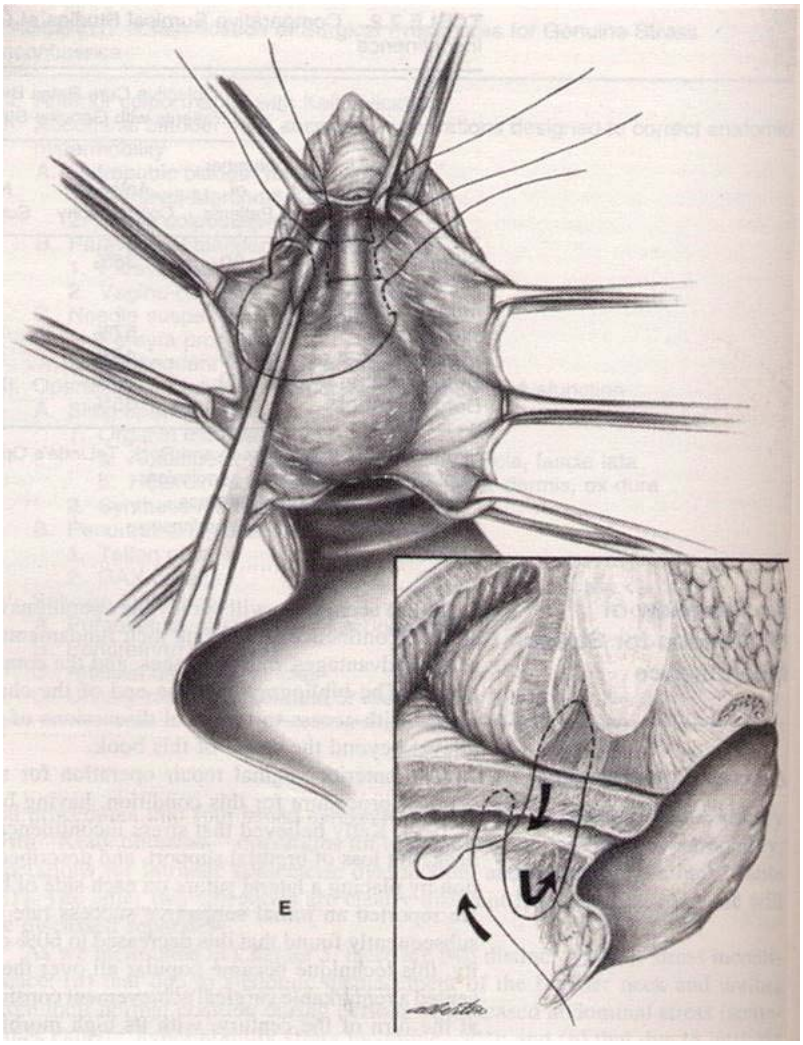
prolapse through the weakened support. Kelly plication sutures were used to repair the pubo-cervical septal defect and support the proximal urethra and bladder neck. Results were poor due to many factors: poor diagnostic techniques, inadequate understanding of the anatomic problem, patient selection, and surgical technique.

Photo of Kelly plication repair:



Needle suspension procedures (Stamey, Gittes, and Peyrera)

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These procedures attempted to suspend the bladder neck via a vaginal approach. This was achieved by either using sutures or a graft to suspend the bladder neck. These procedures were more popular in the urology community. Results were very difficult to interpret due to the different surgical techniques, patient selection, and pre-operative evaluation. These techniques never gained popularity due to the inconsistent results.

Retropubic operations for SUI (Marshall Marchetti Krantz (MMK), Burch Colposuspension and Paravaginal defect repair).

These procedures initially were performed through an abdominal incision and then they were later modified and performed laparoscopically. Both the Burch and MMK procedures require "direct access" to the tissues surrounding the bladder and urethra and are deemed "major" surgical cases that involve an abdominal incision and wide vaginal dissection. This extensive surgery is associated with a significant risk of wound complications, bleeding, and genitourinary tract injury including damage to the ureter, bladder, and urethra (Stanton 1985). . Median surgical times are typically in excess of 2 hours, hospital stay averages 2-3 days, and prolonged catheter drainage is usually required. Most of my young, ambulatory women with primary stress incontinence are unwilling to take 6 weeks off from work and their family obligations to recover from these surgical interventions.

The MMK was an abdominal retropubic procedure that suspended the peri-uerthral tissue to the back of the symphysis pubis. The sutures were anchored into the periosteum of the bone. Problems were osteitis pubis, damage to the blood and nerve supply of the urethra, and a non-mobile urethra.

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The paravaginal repair was a procedure to repair the lateral tear between the vagina and lateral pelvic sidewall in an attempt to recreate the vaginal hammock that supported the urethra. Results varied and this procedure never gained universal adoption in the surgical management of SUI.

The Burch was a procedure which supported the urethra by elevating the paravaginal fascia at the mid urethra and bladder neck to coppers ligament. This procedure became the gold standard to which all incontinence procedures are compared. However, this was an abdominal procedure that required hospitalization and long recovery. It is considered major surgery. The results were very good but it failed in the low pressure urethra or the severe intrinsic sphincter deficiency patient. Patients also required a suprapubic catheter to manage post-operative voiding.

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Photo of a Marshal Marcetti Krantz repair:

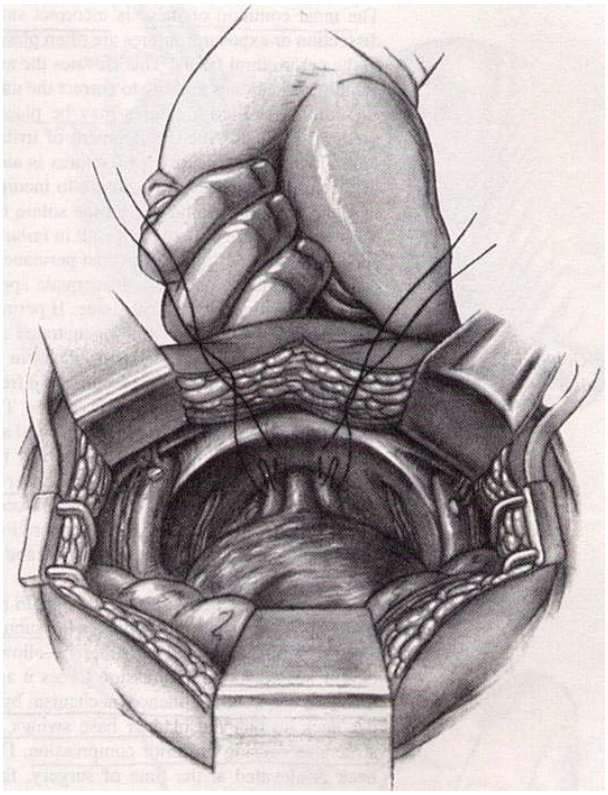

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Photo of a Burch repair:

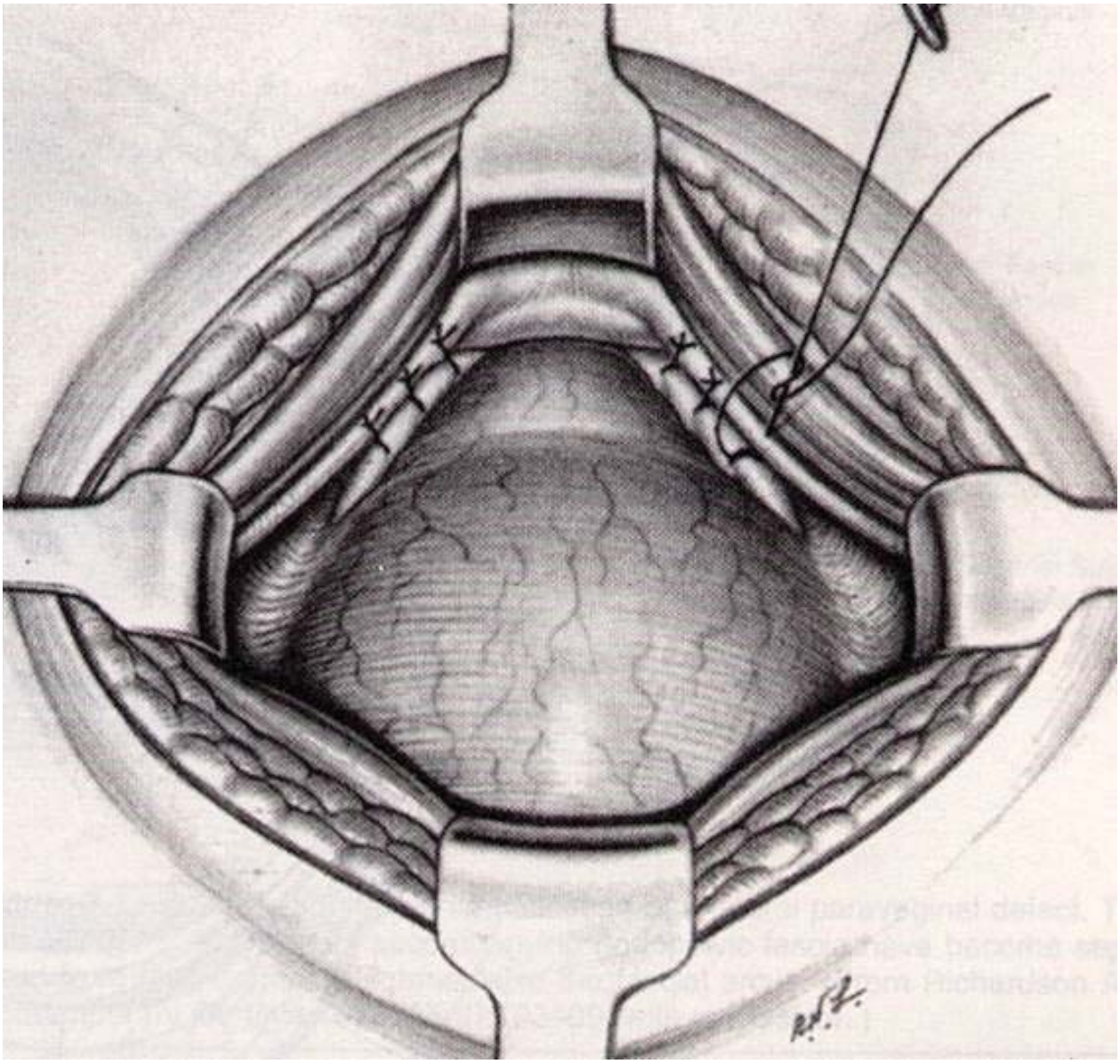

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Photo of combined Burch and Paravaginal repair:

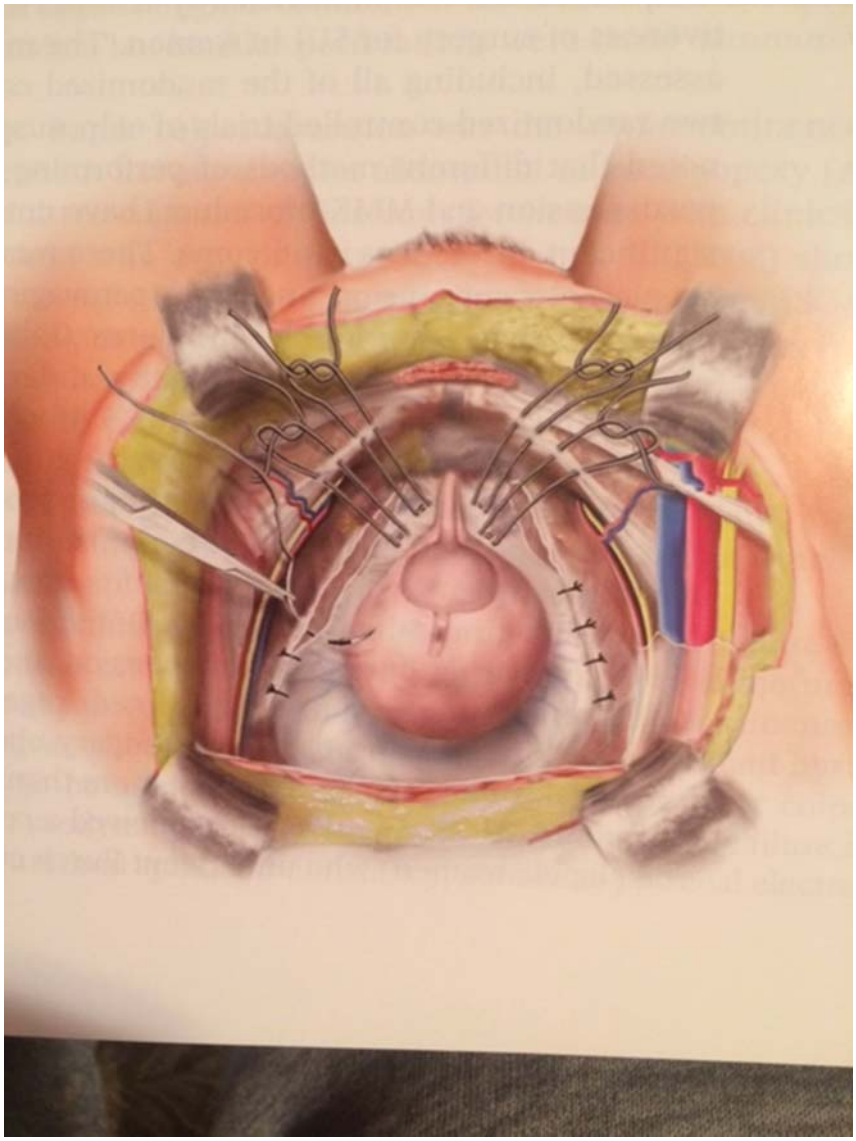

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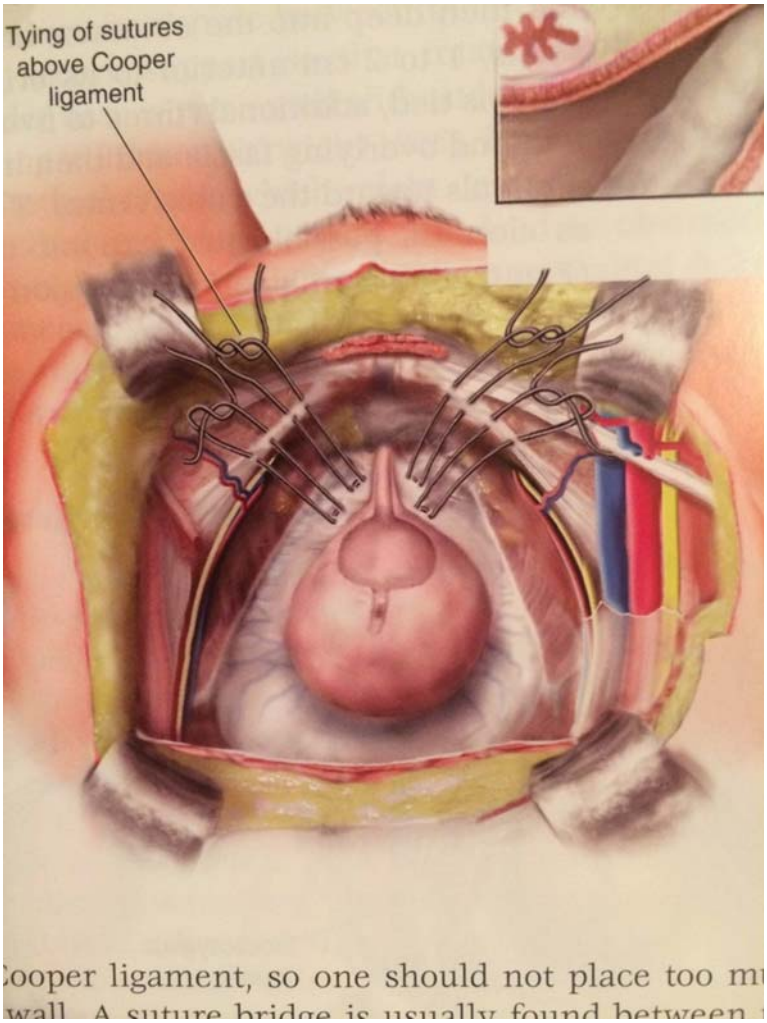
Photo of a Burch repair:



Slings are vaginal procedure designed to re-support the mid-urethra to correct SUI. They can be cadaveric fascia, rectus fascia, biologic material, or synthetic polypropylene mesh.

Cadaveric fascia was used for a short time but results were very inconsistent and it lost its popularity to the rectus fascia sling which is still used under certain conditions.

Rectus fascia slings are used under certain conditions when a patient cannot tolerate mesh or does not want a mesh sling. It is a more difficult operation, requires a more extensive

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dissection, and result vary based on technique and tensioning. Also, the fascial slings are more bladder neck then mid-urethral. Since fascial slings are placed at the bladder neck and not the mid-urethra, they are more obstructive in nature and therefore susceptible to a higher risk of post- operative complications. These are urinary retention, voiding dysfunction, overactive bladder symptoms and irritative bladder problems. These procedures are more invasive because they also require an abdominal incision to harvest the patient's fascia.

Photo of rectus fascia harvest:

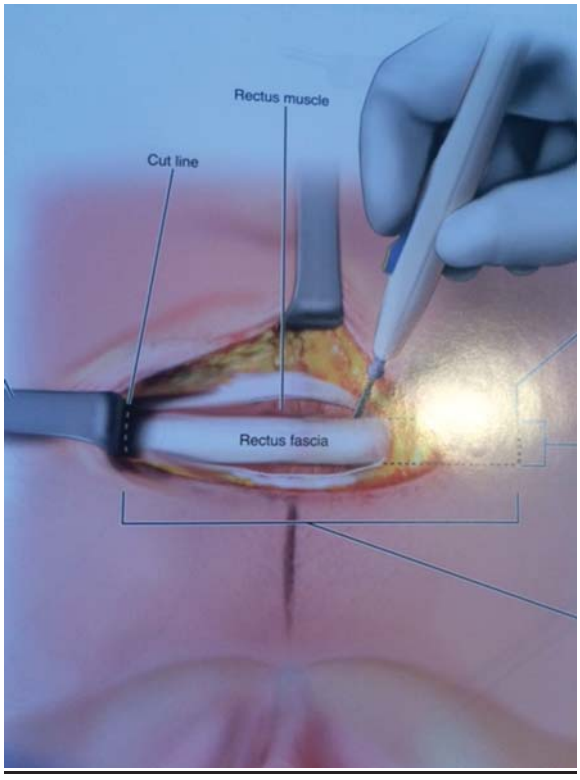

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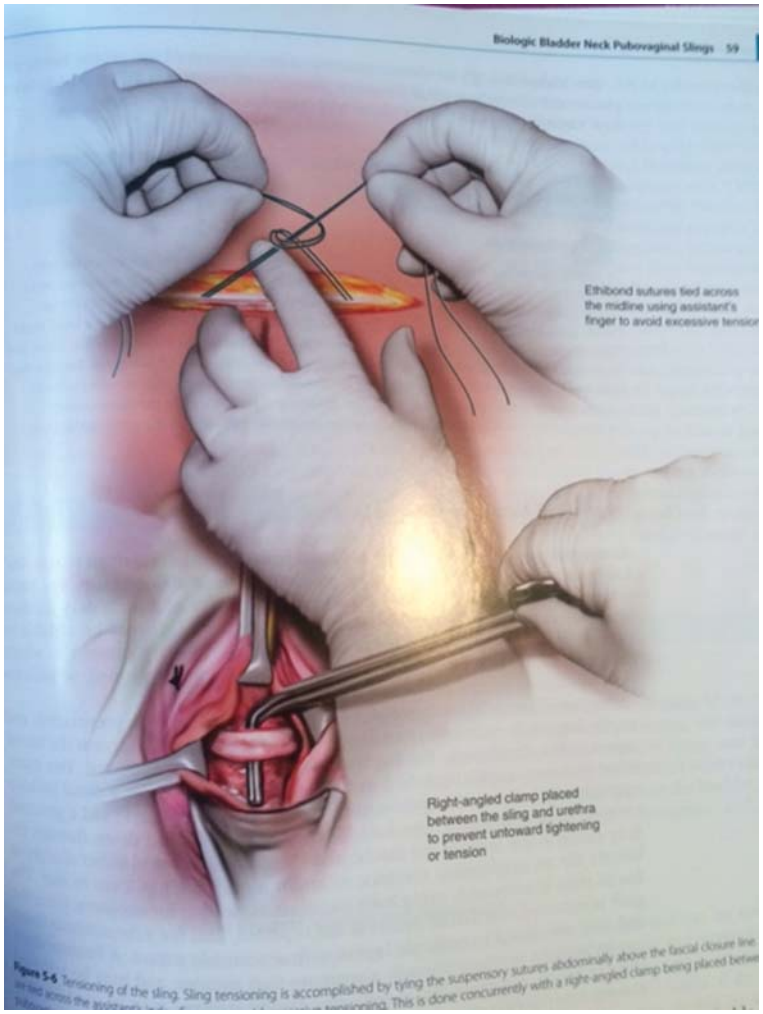
Photo of a fascial sling:



TVT (Tension free vaginal tape): Mid-urethral slings have revolutionized the surgical approach to SUI management. In the opinion of most experts in the field the TVT revolutionized how we manage SUI. It has the advantages of: a minimally invasive outpatient procedure, results comparable to the Burch procedure, 30 min or less operating time, and very rapid patient recovery. The results are reproducible, and it works well in both the hypermobile

and intrinsic sphincter deficiency urethra. The procedure is based on the "integral theory" proposed by Ulmsten and Petros in 1995. The theory is based on the presumption that the pubo-urethral ligaments support the mid-urethra and attach to the pubic bones, acting as a backboard. The backboard allows compression of the mid-urethra during increased intraabdominal pressure thus maintaining continence. The concept states that absence of the backboard support causes loss of the watertight seal and SUI develops. By placing a supportive material under the mid-urethra the backboard action can theoretically be replicated. In designing the tension free vaginal tapes, certain goals were set:

1. To avoid the need for a major abdominal incision and use the vagina as the primary route of surgical access

2. Introduce a stable hammock of support at the level of the mid-urethra and not the bladder neck

3. Provide urethral closure only during episodes of increased intra-abdominal stress and not at rest, thereby reducing the risks of voiding dysfunction

4. Use a sling material that was safe, durable, and did not require harvesting of native tissue

5. Design a system that required minimal tissue dissection, thereby maximally preserving the nerves and surrounding supportive tissue.

6. Design a procedure and technique that is highly reliable and reproducible

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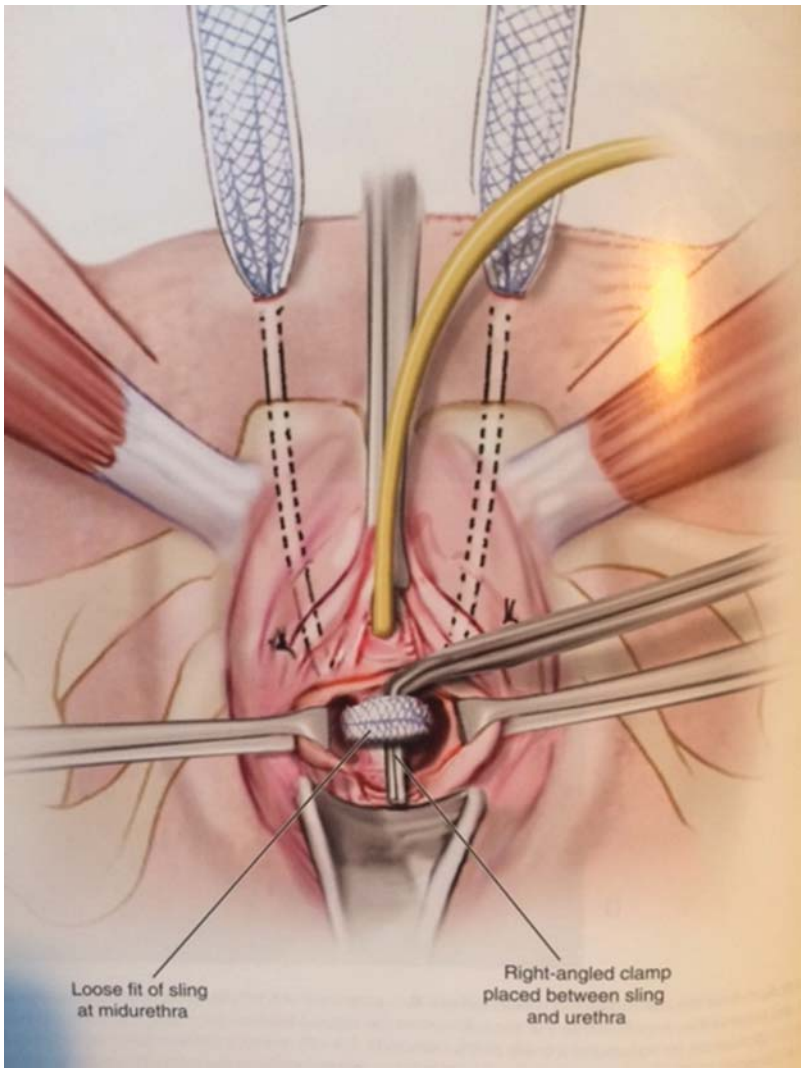
Photo of retropubic TVT: (also showing the loose tensioning technique)



TOT (Transobturator sling): Because retropubic TVT required a blind passage through the retropubic space, inadvertent bladder perforation occurs in 3%-5% of, cases. If there is inadvertent bladder perforation, it does not cause any permanent damage. Routine cystoscopy is performed on all sling procedures and a perforation would be picked up immediately. The TVT introducer would be removed, the urethral catheter guide would displace the bladder and

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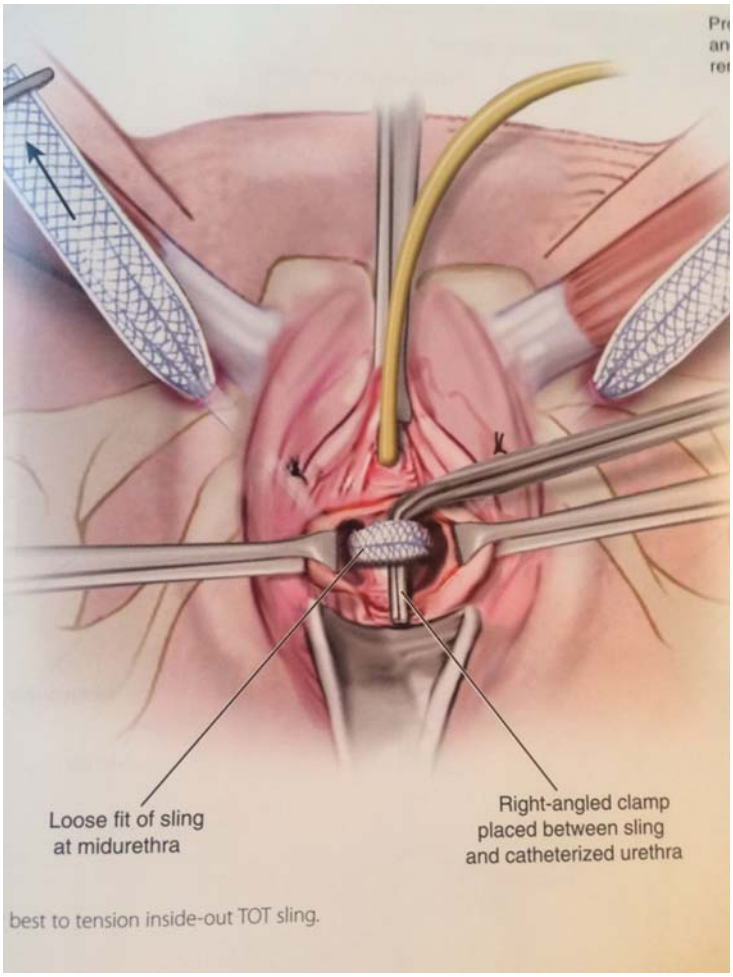
urethra away from the area, and the introducer would be placed more lateral to the first pass. Again, cystoscopy is performed and if correct placement is assured then the sling is placed. Post-operative management is exactly the same and we do not require prolonged catheterization in these situations. Also, vascular and bowel injuries, albeit rare, were reported that resulted in significant morbidity and mortality. In hope of avoiding these complications, Delorme described the trans-obturator technique in 2001.

Photo of transobturator sling:



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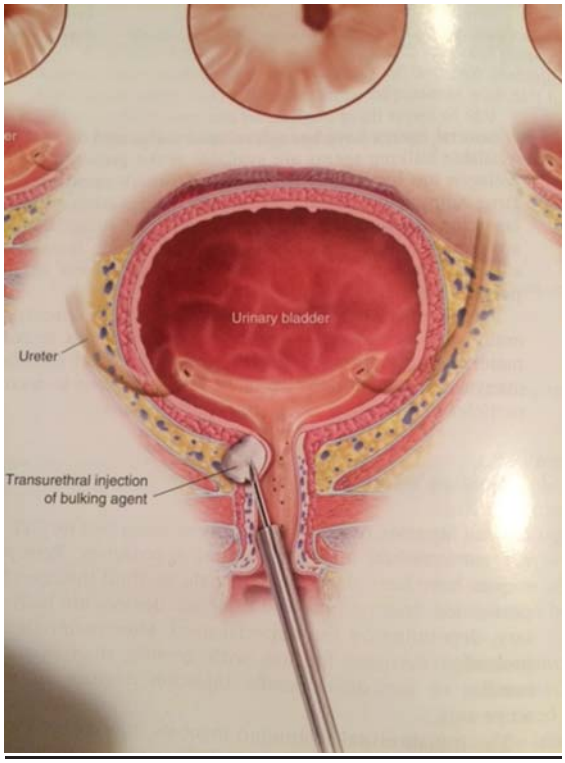
Alternative procedures:

There have been attempts to modify the procedure by using freezing or radiofrequency to treat the periurethral tissue and recreate the support. None of these procedures have gained support. The results are poor and they have a higher complication/failure rate.

Periurethral bulking agents: This is a cystoscopic directed procedure where certain materials are injected into the mucosa of the urethra at the level of the urethra-vesical junction. It attempts to increase urethra resistance by coapting the urethral mucosa. It is not typically used as a primary procedure but more as an adjunct. It does not work well in the hypermobile urethra and may help in the patient with ISD. There is debate over the type of material to be used hence the inaccuracy in the results.

Peri-urethral bulking agent injection:



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Results and References:

The TVT procedure is one of the most studied procedures in gynecology. The literature supports its use overwhelmingly as safe, minimally invasive, with excellent results comparable to any other procedure, has high patient satisfaction, and strong clinical outcomes. Complication rates are low compared to the more invasive procedures. The results are very reproducible regardless of the surgeon performing the procedure.

The Cochrane Library published a meta-analysis (based on 62 studies) showing short-term cure rates between 73% and 82%. The largest randomized controlled study comparing retropubic and transobtrurator slings (Trial of Mid-Urethral Slings [TOMUS]) showed subjective and objective cure rates of 62% and 78% respectively. Two prospective cohort studies reporting 7-year and 11-year follow-up reported subjective cure rates of 85% and 77% respectively. There is no question that the literature is abundant with data to support the use of TVT in the treatment of SUI.

There are many very well designed studies that have shown the efficacy and safety of the TVT procedure. I have highlighted a few comparisons to demonstrate these findings.

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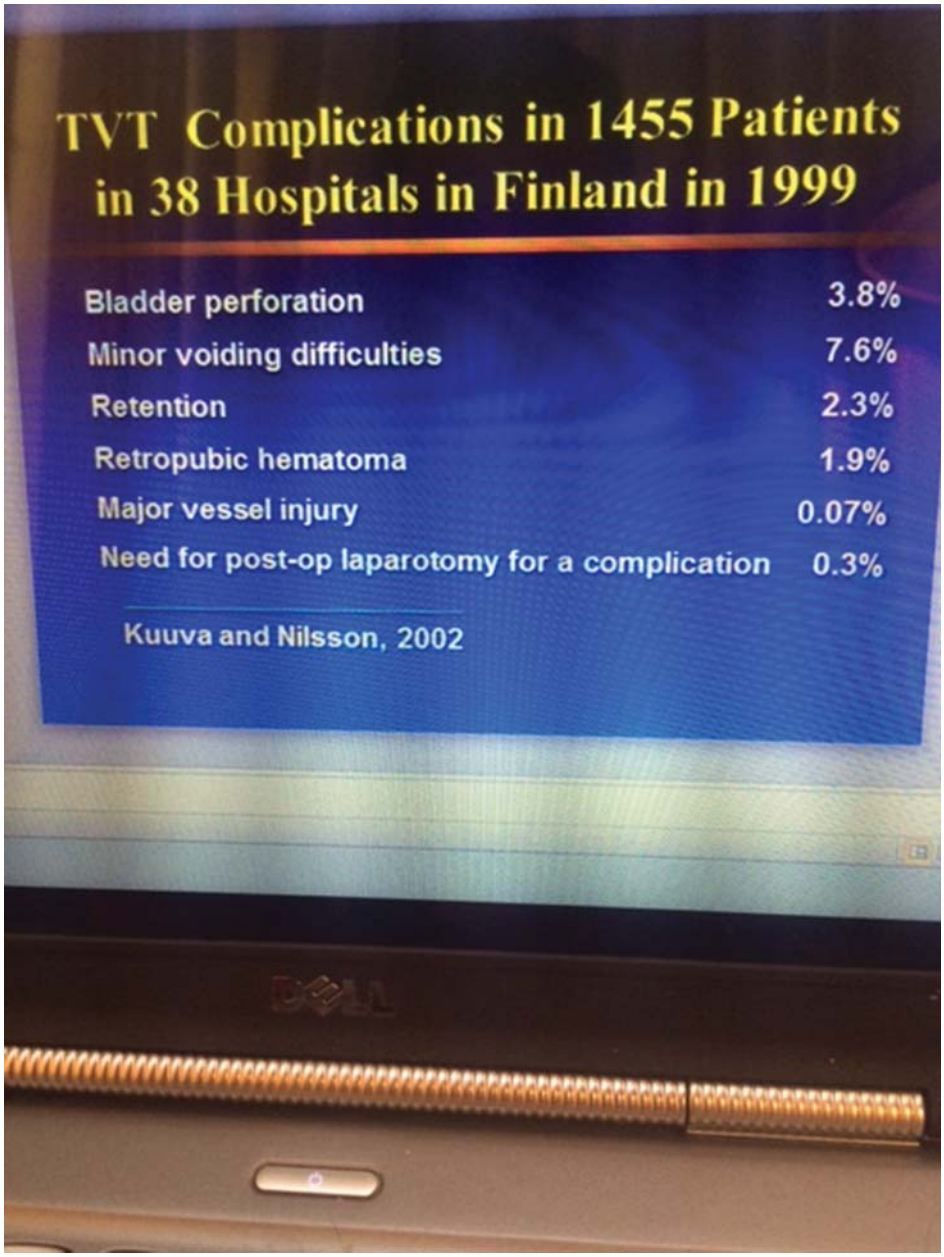

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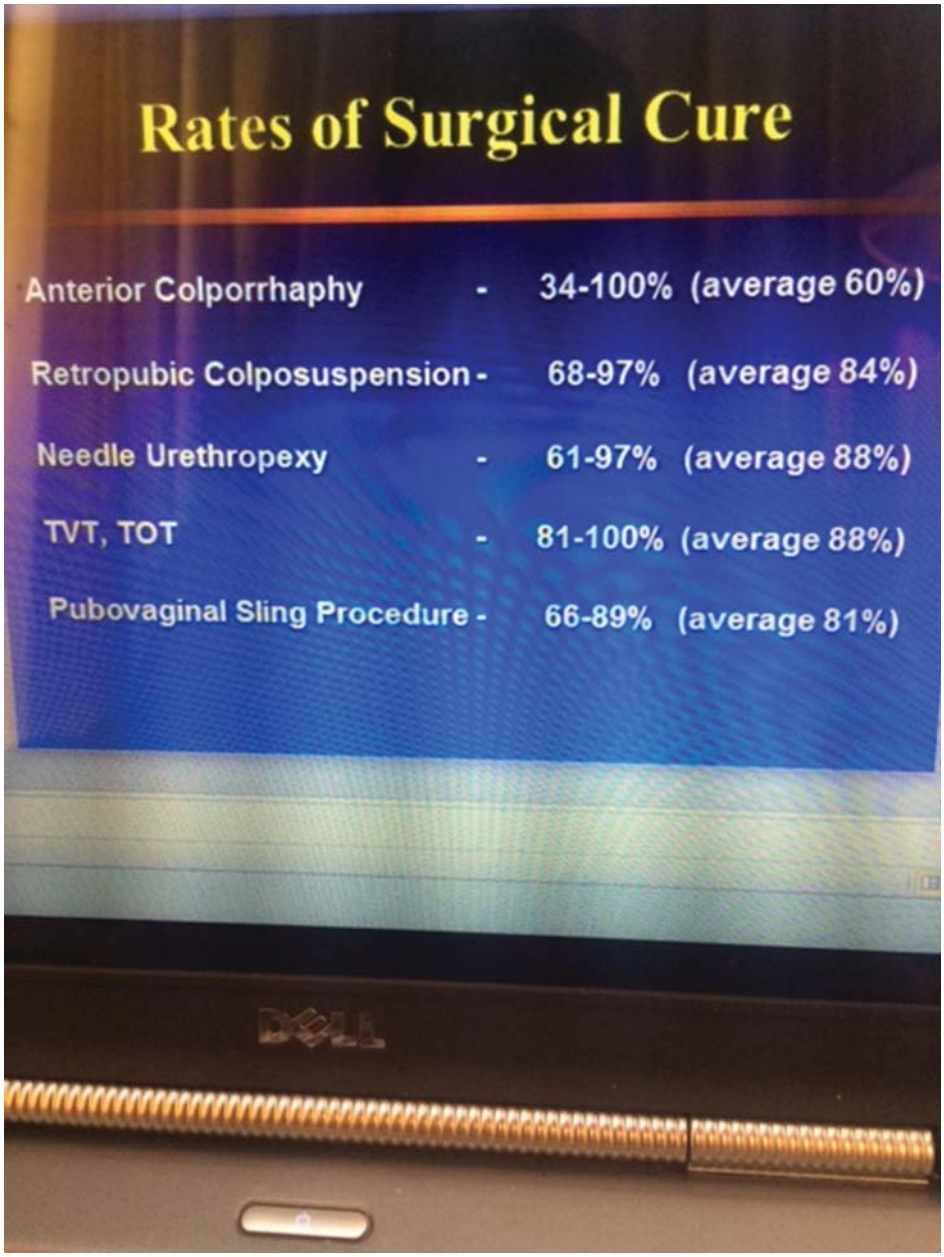

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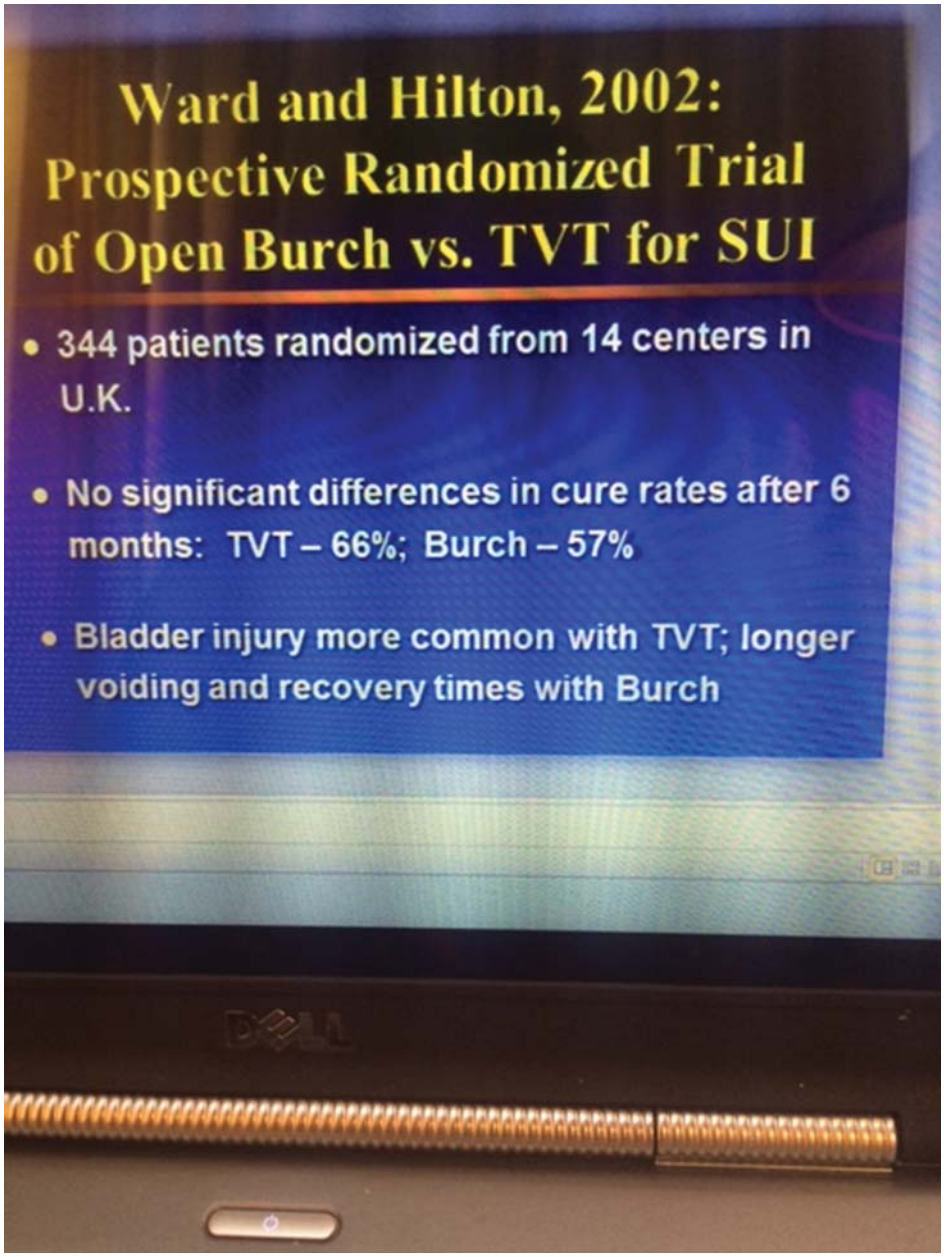

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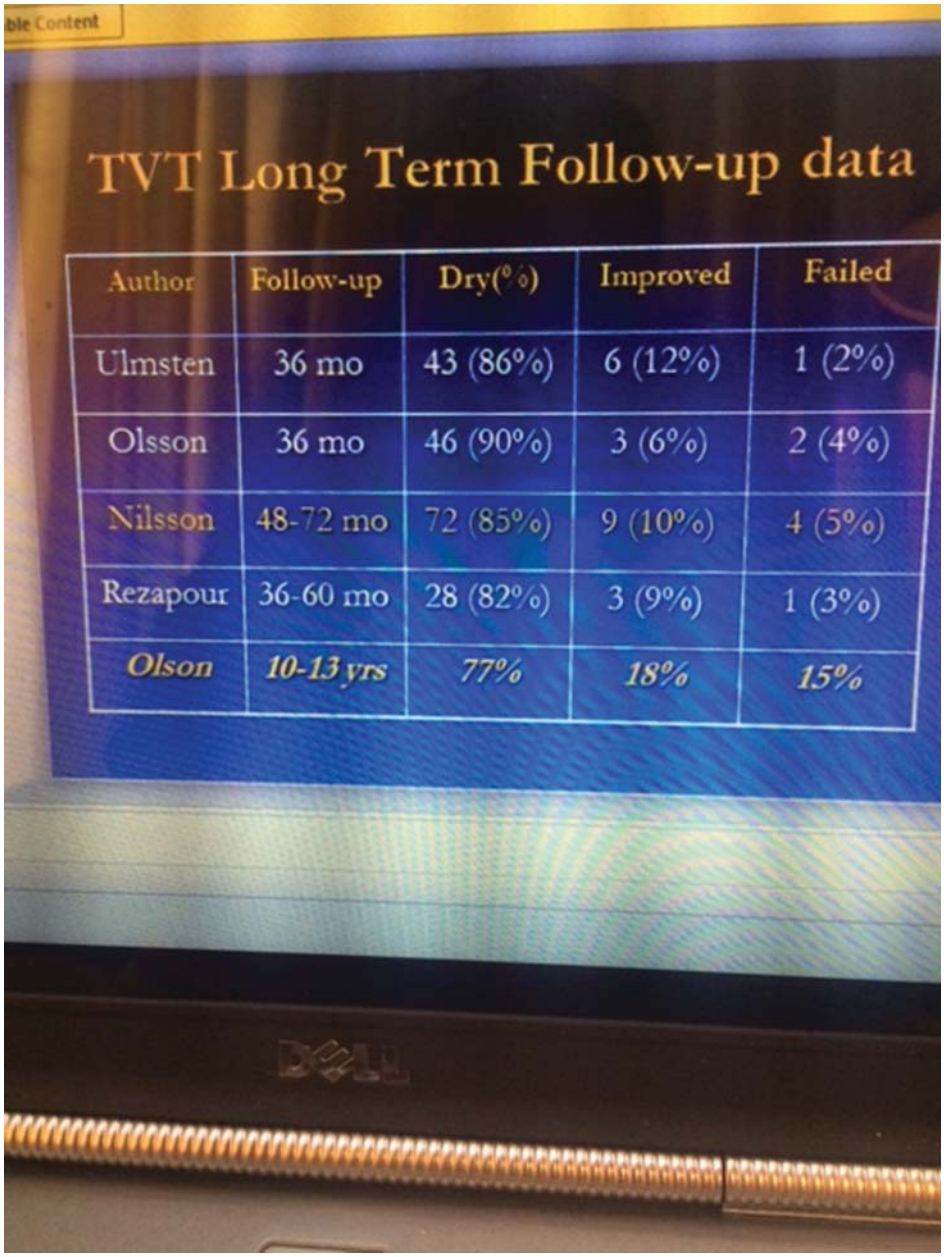

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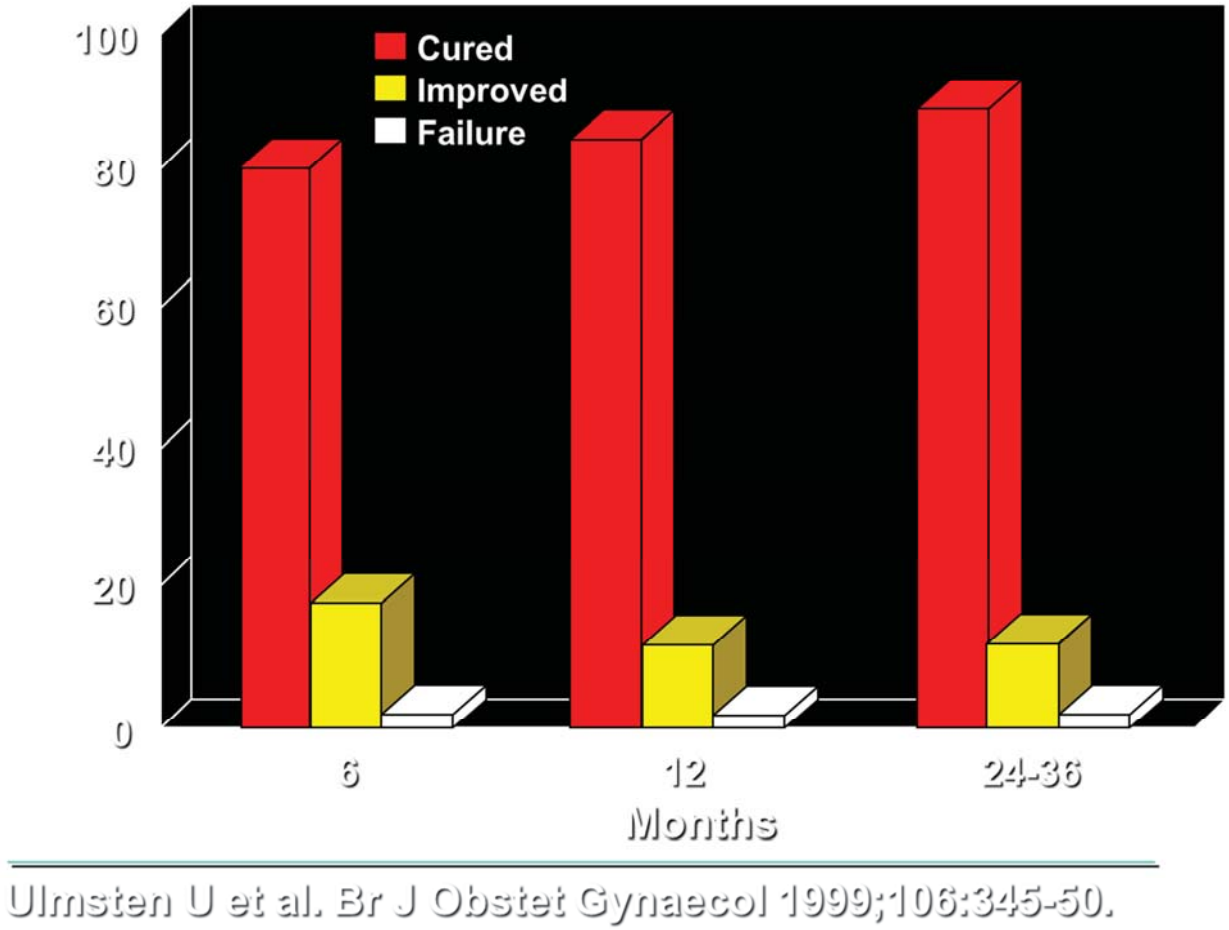

Company Training:

Ethicon/Gynecare did an excellent job of educating surgeons on the use of their products. As mentioned above in this document, I served as lead faculty on many training sessions. Thus, I have an intimate understanding of what the reasonably prudent pelvic floor surgeon should know about the risks and benefits of pelvic floor procedures, the adequacy of the warnings in IFUs, the management of mesh complications, and the well-known risks that are associated with any pelvic floor surgery. It is well known by all pelvic floor surgeons that

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any surgery for stress urinary incontinence or pelvic organ prolapse, with or without the use of mesh, can potentially cause complications that can be temporary or permanent, including but not limited to: pelvic pain, dyspareunia (pain with sexual intercourse), scarring, vaginal narrowing, leg/groin pain, urinary retention and other voiding problems. The process would begin with the representatives in the field surveying qualified surgeons that might be interested in the use of these devices. A qualified surgeon would be a urogynecologist or gynecologist who is experienced and knowledgeable in the surgical management of SUI. Hence, that is a major portion of their practice. They would be given information on the products, the IFUs, and clinical data to review before their training session. The training session would be two days Friday night an in depth discussion between faculty and participants' about indications, contraindications, technique, complications and management of the complications. Saturday would be a full day in the cadaver lab 7am-5pm. A didactic presentation followed by a cadaver lab where every participant, under the supervision of the faculty member, would implant the device over and over again until the faculty member and participant were satisfied with the objectives. The participants would receive a certificate verifying their attendance at the course. Faculty members would then meet with the Ethicon/Gynecare representatives and give them an evaluation of all the participants, specifically those that were felt to be deficient or weak in their technique or knowledge. Upon departure all participants were given our contact info to call if they had any questions or problems. They were also offered a preceptor to come to their institution and observe with their first few cases if they desired.

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Surgeon Credentialing:

Credentialing is done by the hospital credentialing committee, not by Ethicon/Gynecare. Every hospital had its own method for credentialing. At our institution, surgeons were credentialed based on their surgical practice, volume and past surgical history. Once they were credentialed they must be observed by an experienced TVT surgeon for their first 5 cases.

Adequacy of Company IFU and Patient Brochures:

Ethicon/Gynecare had very detailed Instruction for Use (IFU) with all their sling products. They are very detailed and self-explanatory on all aspects of the procedures. We also made it a point to go over the IFU in detail during training sessions. They detailed all the issues related to warnings and precautions associated with the procedures. All participants were given the IFU as well. The company also offered detailed brochures with resources available to the patients.

In summary, my opinion of the TVT procedure is very favorable. It is a simple, minimally invasive technique, excellent results, excellent patient satisfaction and outcomes. The risks are minimal compared to the more invasive surgeries we performed before the introduction of TVT. The complications are easy to manage and usually have good results as well. All patients are consented and understand the risks, benefits, options, complications, side effect, and results. In my opinion it is the first line surgical option for SUI. The large volume of data available support this idea and it continues to be the procedure of choice in the majority of surgeons that perform SUI surgeries.

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Malignant potential of mesh:

The malignant potential of implanted mesh in humans has been raised by plaintiffs. This can be attributed to animal studies done in 1958 by Dr. Oppenheimer. He demonstrated the development of sarcomas in rats implanted with sheets of plastic. However, more recent animal studies implanting monofilament and multifilament polypropylene mesh in mice, did not corroborate these findings. This phenomenon was related to the implanted materials physical traits with discs and sheets including pure metal, polymers, and glass being the most carcinogenic. These solid materials lose their carcinogenicity when they are implanted in porous or woven forms. An epidemiologic study by the International Agency for Cancer Research (IARC) in 2000 concluded that there is no evidence of tumorgenicity of metallic or synthetic implants in humans.

Surgeons at the Cleveland Clinic reviewed their mid-urethral synthetic slings performed between 2004 and 2013. During this period, 2,361 synthetic slings were performed and followed for 5-6 years. No sarcomas were found and their incidence of malignancy after mid-urethral sling was 0%. Their conclusion was there is no support for any association between polypropylene mesh used in mid-urethral slings and the development of malignancy in humans.

Surgeons at the Mayo Clinic reviewed their data from 2002-2012. During this period, 2,474 synthetic slings were placed. Median follow-up was 5 years. Their conclusion was that the development of pelvic malignancy after a mid-urethral synthetic sling is rare and unlikely to be secondary to foreign body reaction from implanted material.

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The American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU), answered this question by stating 'Tumors related to the implantation of surgical grade polypropylene for mid-urethral slings in humans have never been reported. There is no compelling evidence supporting human malignant transformation related to polypropylene despite millions of individuals implanted with various forms of this material spanning well over a half century world-wide.'

To date, there is no level I scientific data to conclude there is a correlation between the development of malignancy in humans with the implantation of polypropylene mesh products. They should be considered safe until scientific data proves otherwise.

Pore size and degradation issues:

Type I mesh is monofilament and manufactured with a pore size greater than 75 microns. Mesh used in SUI management is polypropylene Type 1 knitted, monofilament and macroporous.

Macroporous defines pores that are greater than 75 microns and is important for many reasons. Such construction promotes resistance to infection by allowing macrophages to enter the pores. Macrophages cannot enter pores that are less than 10 microns. Such design also allows greater type III collagen deposition, greater capillary penetration, and greater attachment strength.

Knitted mesh has the highest porosity, lowest volume and largest interstices. Porosity allows the growth of fibroblasts around monofilaments without contraction bridges. This minimizes the foreign body reaction. The flexibility of the fiber in the lightweight macroporous

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graft facilitates a tension free repair and helps prevent stiffness in the vagina after augmentation.

The biology of prosthetic implant incorporation is accomplished in stages. By day 3 there is inflammation first exudative and then cellular. Polypropylene is the least inflammatory. By day 10 there is fibroblast ingrowth and by week 6 complete ingrowth. The prosthetic strength doubles from week 3 to week 12.

The Prolene TVT mesh is considered to be an Amid Type 1 mesh, and is commonly referred to as large-pore and lightweight mesh. The initial TVT trials with Prolene mesh by Ulmsten, showed no adverse reaction. Specifically, there was no indication of unacceptable rates of mesh infection, rejection, host tissue reaction, or impaired healing. Heavier meshes have greater and more prolonged inflammation. They have greater scar plating and less elasticity once incorporated. Also, there is evidence of increased cell turnover ongoing inflammation and remodeling at one year.

There is likewise no clinical significance to claims of alleged particle loss and mesh degradation over time. Such claims are not supported by any level 1 evidence, nor have I experienced any complications attributable to alleged particle loss or degradation in my 20 years of clinical practice.

Ethicon still sells both mechanically cut and laser cut TVT in order to satisfy surgeon preferences. There has been rigorous clinical data from implants prepared using the 2 different techniques. There has been robust opportunity to assess for any difference in outcomes. None

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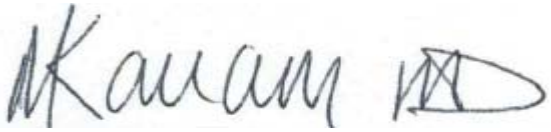
have been observed. Overall, this theoretical risk has led to no measurable clinical effect or risk.

I reserve the right to change my opinion if data contrary to the available data is presented.

All photos were from Baggish and Karram; Atlas of Pelvic Anatomy and Gynecology, Surgery for Urinary Incontinence; Dmochowski, Karram, and Reynolds, and Urogynecology and Reconstructive Surgery; Walters and Karram.



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